

## IN THE CLAIMS:

1. (currently amended) An effervescent pharmaceutical formulation for the sustained and controlled oral administration of a pharmaceutically effective amount of a drug selected from the group consisting of a calcium channel blocker, an ACE inhibitor, a narcotic analgesic or analogues or combinations thereof, said formulation comprising microcapsules having a D50% between about 100 nm and 900nm in which the drug is entrapped in a biodegradable polymer and in which the pH of the formulation is adjusted to optimize delivery of the drug, wherein the formulation is adapted to disperse upon addition of water to form and effervescent drink.
2. (Cancelled)
3. (previously presented) An effervescent pharmaceutical formulation according to Claim 1, wherein the formulation is used to delivery the drug to a patient a on a once-daily basis so as to achieve a therapeutic effect over a substantially 24 hour period.
4. (Cancelled)
5. (previously presented) An effervescent pharmaceutical formulation according to claim, wherein the drug loading of the microcapsules ranges for about 10% to 70% by weight.
6. (currently amended) An effervescent pharmaceutical formulation for the sustained and controlled oral administration of a pharmaceutically effective amount of a drug selected from a calcium channel blocker, an ACE inhibitor, a narcotic analgesic or combination thereof, the formulation comprising drug-loaded biodegradable microcapsules having a D 50% between about 100nm, and 900nm and a drug loading which ranges for about 10% to 70% by weight and wherein the pH of the formulation is adjusted to optimize delivery of ~~or~~ each drug.
7. (previously presented) An effervescent pharmaceutical formulation according to Claim 6, wherein can be used to deliver the drug to a patient a once-daily basis so as to achieve a therapeutic effect over a substantially 24 hour period.
8. (previously presented) An effervescent pharmaceutical formulation

according to claim 1, wherein the microcapsules have a D 50% between about 200nm, and 400nm

9. (previously presented) An effervescent pharmaceutical formulation according to claim 1, wherein the drug loading of the microcapsules ranges from about 20% to 50 by weight.

10. (previously presented) An effervescent pharmaceutical formulation according to claim 1, wherein the drug is selected from diltiazem, verapamil, nifedipine, nimodopine, nicardipine, hydromorphone, codeine sulfate, oxycodone, dihydrocodeine tartrate, oxycodone morphine, fentanyl, sufentanil, oxymorphone, buprenorphine, captopril, enalapril, lisinopril and mixtures thereof.

11. (previously presented) An effervescent pharmaceutical formulation according to Claim 10, wherein the drug is a mixture of nifedipine and hydromorphone.

12. (previously presented) A pharmaceutical formulation according to claim 1, wherein the microcapsules comprise a polymer matrix, said polymer matrix comprising a polymer selected from the group consisting of polylactide; polyglycolide; poly(lactic acid-co-glycolic acid); poly( $\epsilon$ -caprolactone); poly(hydroxybutyric acid); polyortho-esters; polyacetals; polydihydropyrans; polycyanoacrylates; polypeptides; cross-linked polypeptides; and stereoisomers, racemic mixtures, co-polymers and polymer mixtures thereof.

13. (previously presented) A pharmaceutical formulation according to Claim 12, wherein the polymer matrix comprises poly-D,L-lactide.

14. (previously presented) A pharmaceutical formulation according claim 1, wherein the release profile measured in accordance with the Paddle Method of U.S. Pharmacopoeia XX at 37°C and 75 rpm for each drug is substantially as follows:

- a) 10-30% release within 2 hours after administration;
- b) 30-60% release within 4 hours after administration;
- c) 60-80% release within 2 hours after administration; and
- d)  $\geq$  80% release within 24 hours after administration.

15. (previously presented) A pharmaceutical formulation according any one of Claims 1, wherein the release profile measured in accordance with the Paddle Method of U.S. Pharmacopoeia XX at 37°C and 75 rpm for each drug is substantially as follows:

- a) 10-40% release within 1 hours after administration;
- b) 20-60% release within 4 hours after administration;
- c) 40-80% release within 8 hours after administration; and
- d)  $\geq$  80% release within 16 hours after administration.

16. (previously amended) A method for manufacture of microcapsules according to Claim 1, which comprises the step of:

a) dissolving or dispersing a drug and a biodegradable polymer in a solvent to form a mixture;

b) microfluidising said mixture into an external phase to form an emulsion in which the emulsion droplets have a mean diameter less than 1 mm; and

c) stirring said emulsion to form microcapsules having a size (D 50%) between about 100 nm and 900nm.

17. (Cancelled)

18. (Cancelled)

19. (Cancelled)

20. (Cancelled)

21. (previously presented) The effervescent pharmaceutical formulation of Claim 1, wherein the drug is diltiazem or a combination of diltiazem and a narcotic analgesic or an ACE inhibitor and wherein the pH of the formulation is greater than 7.

22. (previously presented) The effervescent pharmaceutical formulation of Claim 1, wherein the drug is hydromorphone or a combination of hydromorphone and a calcium channel blocker or an ACE inhibitor and wherein the pH of the formulation is less than pH 6 or greater than pH 7.

23. (new) The formulation of Claim 1 wherein microcapsules are prepared from an emulsion comprising a suspension medium and suspended therein droplets having a mean droplet diameter of less than 1 micron, said droplets comprising the drug and said encapsulating polymer.

24. (new) The formulation of Claim 23 wherein said biodegradable polymer is selected from polylactide, polyglycolide, poly(lactic acid-co-glycolic acid), poly( $\epsilon$ -caprolactone), poly(hydroxybutyric acid); polyorthoesters; polyacetals, polydihydropyrans, poly cyanoacrylates; polypeptides, cross-linked polypeptides, and stereoisomers, racemic mixtures, co-polymers and polymer mixtures thereof.

25. (previously presented) The formulation according to claim 24, wherein said drug is selected from the consisting of diltiazem,

verapamil, nifedipine, nimodopine, nicardipine, hydromorphone, codeine sulfate, oxycodone, dihydrocodeine tartrate, oxycodone morphine, fentanyl, sufentanil, oxymorphone, buprenorphine, captopril, enalapril, lisinopril and mixtures thereof.

26. (previously presented) The formulation according to Claim 25 wherein the biodegradable polymer is poly-D,L-lactide.

27. (previously presented) The formulation according to Claim 26 wherein said drug is a mixture of a calcium antagonist and a narcotic analgesic.

28. (previously presented) The formulation according to Claim 27 wherein said calcium antagonist is diltiazem.

29. (previously presented) The formulation according to Claim 27 wherein said calcium antagonist is nifedipine.